TARGETED AND REGIONAL CELLULAR ABLATION IN ZEBRAFISH

ABSTRACT OF THE DISCLOSURE

A system including: (i) a methodology for targeted cellular ablation in zebrafish; (ii) a methodology for regional cellular ablation in zebrafish. These methodologies are used to identify genetic components that regulate cellular regeneration and to identify drug compounds that influence cellular regeneration for the purpose of developing therapies for degenerative conditions. Transgenic zebrafish disclosed herein contain transgenic constructs composed of: (i) cell and/or tissue-type specific regulatory elements (e.g. promoter and/or enhancer regions) which delimit expression of operably linked gene product(s) to discrete cellular populations; (ii) a gene product that promotes cellular ablation composed of a pro-drug conversion system capable of converting nontoxic pro-drugs into cytotoxic drugs, which is expressed alone or in connection with; (iii) a reporter gene product that allows selective detection of cells expressing the reporter - both prior to (initial cells) and following cellular ablation (regenerated cells). Here we describe genetic delivery of a pro-drug converting system in order to enable targeted cellular ablation in zebrafish. Transgenic zebrafish of this invention provide a high-throughput system for genetic dissection of the process of cellular regeneration and, compound screening for the discovery of drugs capable of promoting cellular regeneration.